SUPPORT FOR THE AMENDMENTS

The present amendment cancels claims 25-29, and amends claim 21.

Support for the amendment to claim 21 is found at specification page 10, lines 14-24, and page 18, line 18, as well as claims 25-27.

It is believed that these amendments have not resulted in the introduction of new matter.

REMARKS

Claims 21-24, 30, 31, 54 and 56 are currently pending in the present application. Claims 25-29 have been cancelled, and claim 21 has been amended, by the present amendment.

Applicants wish to extend their appreciation to Examiner Peselev for the helpful and courteous discussion held on May 8, 2008, with their undersigned Representative. During the meeting, the prior art rejections, as well as the evidence presented in Figures 1 and 2 of the present specification, were discussed. The content of this discussion is reflected in the remarks set forth herein.

The rejection of claims 21-31, 54 and 56 under 35 U.S.C. § 103(a) as being obvious over either Izumi (JP 11-060592) or Shin (JP 00-191685) in view of Endo (U.S. Patent 5,569,464) is respectfully traversed in part, and obviated by amendment in part with respect to the amendment to claim 21, which incorporates the limitation of a positive-charge-providing aliphatic amine selected from the group consisting of stearylamine and oleylamine.

Izumi describes an anticancer medicine comprising a cholestanyl glycoside having a Fuc-Gal- sugar moiety (See e.g., abstract). Unlike the claimed invention, Izumi fails to disclose or suggest incorporating a cholestanyl Fucα1,3Gal- glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing aliphatic amine selected from the group consisting of stearylamine and oleylamine.

Shin describes an anticancer agent comprising a cholestanyl glycoside having a GlcNAc-Gal- sugar moiety (See e.g., abstract). Unlike the claimed invention, Shin fails to disclose or suggest incorporating a cholestanyl GlcNAcβ1,4Gal- glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing aliphatic amine selected from the group consisting of stearylamine and oleylamine.

Endo describes incorporating various hydrophilic or lipophilic active agents, including carcinostatic agents, into a liposomal composition comprising a phospholipid (e.g.,

dipalmitoylphosphatidylcholine) and a positive-charge-providing substance (e.g., an aliphatic amine, such as stearylamine) for the purpose of controlled and targeted release of the active agents, as well as the stabilization of unstable active agents (See e.g., column 1, lines 20-24, column 2, lines 37-40 and 49-50, column 3, lines 57-59 and 64-65, and column 4, lines 51-52). The carcinostatic agents described in Endo include antitumor antibiotics (i.e., mitomycin, doxorubicin or adriamycin), antimetabolites (i.e., methotrexate and tegafur), a platinum compound (i.e., cisplatin), and a vinca alkaloid (i.e., vincristine) (See e.g., column 4, lines 51-52).

Endo fails to provide sufficient motivation and guidance to direct a skilled artisan to particularly select the claimed cholestanyl Fucα1,3Gal- glycoside anticancer agent and the claimed cholestanyl GlcNAcβ1,4Gal- glycoside anticancer agent from either the tremendously broad genus of hydrophilic or lipophilic active agents, or the preferred carcinostatic agents, described therein.

Even if sufficient motivation and guidance is considered to have been provided by Endo to direct a skilled artisan to particularly select the claimed cholestanyl Fucα1,3Gal- glycoside anticancer agent from the cholestanyl Fuc-Gal- glycoside of Izumi and/or the claimed cholestanyl GlcNAcβ1,4Gal- glycoside anticancer agent from the cholestanyl GlcNAc-Gal- glycoside of Shin for incorporation into the liposomal composition of Endo, such a case of obviousness is rebutted by a showing of unexpected results in the comparative experimental data presented in Figures 1 and 2 of the present specification.

Applicants have discovered that the claimed liposomal composition comprising: the cholestanyl glycoside according to formula (1), which has a sugar moiety selected from the group consisting of GlcNAcβ1,4Gal- and Fucα1,3Gal-; the phospholipid; and the positive-charge-providing aliphatic amine, unexpectedly exhibits a remarkable degree of enhanced anti-tumor efficacy.

A general increase in antitumor efficacy attributable to incorporating cholestanyl anticancer agents into a liposomal composition may be reasonably expected, due to the stabilization and

controlled/targeted delivery thereof (See e.g., the comparative experimental data of "Chol" and "Chol-Lipo" illustrated in Figures 1 and 2).

However, the presently claimed cholestanyl GlcNAcβ1,4Gal- glycoside and cholestanyl Fucα1,3Gal- glycoside anticancer agents surprisingly exhibit a drastically enhanced antitumor efficacy far beyond that which may be reasonably expected by the incorporation thereof into a liposomal composition (See e.g., the comparative experimental data of: "GlcNAcβ1,4GalChol" and "GlcNAcβ1,4GalChol-Lipo" illustrated in Figure 1; and "Fucα1,3GalChol" and "Fucα1,3GalChol-Lipo" illustrated in Figure 2).

Therefore, while a skilled artisan may have reasonably expected an enhancement in antitumor efficacy by incorporating the presently claimed cholestanol glycoside anticancer agents into the liposomal composition of the present invention, due to the stabilization and controlled/targeted delivery thereof, the remarkable degree of enhanced anti-tumor efficacy actually exhibited by the liposomal composition of the present invention was quite unexpected.

The evidence presented in Figures 1 and 2 of the present specification clearly illustrates that liposomal compositions according to the present invention unexpectedly exhibits a drastically enhanced antitumor efficacy.

While the inventive liposomal compositions presented in Figures 1 and 2 comprise dipalmitoylphosphatidylcholine (DPPC) as the phospholipid, Applicants respectfully submit that a skilled artisan would have reasonably expected that phospholipids other than DPPC (e.g., phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidic acid and additional phosphatidylcholines) would exhibit comparable physicochemical properties to those of DPPC based on similarities in their structural formulae.

While the inventive liposomal compositions presented in Figures 1 and 2 comprise stearylamine as the positive-charge-providing aliphatic amine, Applicants respectfully submit that a skilled artisan would have reasonably expected that oleylamine as the positive-charge-providing

aliphatic amine would exhibit comparable physicochemical properties to those of stearylamine based on similarities in their structural formulae.

Accordingly, Applicants respectfully submit that a skilled artisan would have reasonably expected that a liposomal composition comprising phospholipids other than DPPC (e.g., phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidic acid and additional phosphatidylcholines) and oleylamine as the positive-charge-providing aliphatic amine would likewise exhibit drastically enhanced antitumor efficacies similar to those achieved with liposomal compositions comprising DPPC as the phospholipid and stearylamine as the positive-charge-providing aliphatic amine. Applicants are aware of no reason to believe otherwise.

As discussed during the interview, Figures 1 and 2 demonstrate the cell proliferation inhibition (CPI) rate of liposomal compositions according to the present invention to a cultured cancer cell line relative to the concentrations of the claimed cholestanyl GlcNAcβ1,4Gal- glycoside and cholestanyl Fucα1,3Gal- glycoside anticancer agents, respectively, contained within the liposomal compositions (See e.g., page 19, lines 24-27, page 20, lines 1-27, page 21, lines 1-11, page 27, Figure 1, and page 28, Figure 2).

Withdrawal of this ground of rejection is respectfully requested.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

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